AMENDMENTS

Amendments to the claims are set forth in the following listing of claims, which replaces all prior listings of the claims:

1-11. (Cancelled).

12. (Currently amended) A method of treatment for hereditary lymphedema, comprising: ~~the step of~~

administering to a patient with hereditary lymphedema a therapeutically effective amount of a growth factor product selected from the group consisting of vascular endothelial growth factor C (VEGF-C) ~~protein products, vascular endothelial growth factor D (VEGF-D) protein products, VEGF-C~~ gene therapy products, ~~and VEGF-D gene therapy protein products~~

wherein said patient with hereditary lymphedema comprises a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele of the patient, wherein said mutation reduces ligand-mediated signaling of the VEGFR-3 polypeptide encoded by the allele, when compared to VEGFR-3 encoded by a wild-type human VEGFR-3 allele; and

wherein said therapeutically effective amount of said growth factor product is administered locally at a site of edema in the patient.

13-25. (Cancelled).

26. (Withdrawn – currently amended) The method of claim 12 or 37, wherein the mutation results in ~~A purified polynucleotide according to claim 25 wherein the polynucleotide encodes~~ an amino acid sequence that differs from SEQ ID NO: 2 at least one residue selected from the group consisting of residues 843 to 943 and 1009 to 1165 of SEQ ID NO: 2.

27-36. (Canceled)

37. (Currently amended) A method of treatment for hereditary lymphedema comprising:

screening nucleic acid of a patient for ~~The method of claim 12, wherein said patient with hereditary lymphedema comprises~~ a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele of the patient, wherein said mutation reduces ligand-mediated signaling of the VEGFR-3 polypeptide encoded by the allele, when compared to VEGFR-3 encoded by a wild-type human VEGFR-3 allele; and

identifying a patient with said mutation as a hereditary lymphedema patient and administering to said hereditary lymphedema patient a therapeutically effective amount of a growth factor product selected from the group consisting of vascular endothelial growth factor C (VEGF-C) gene therapy products,

wherein said therapeutically effective amount of said growth factor product is administered locally at a site of edema in the patient.

38. (Currently amended) The method of claim 12 or 37, wherein said mutation is a mutation altering a tyrosine kinase domain amino acid sequence of the protein encoded by the VEGFR-3 allele.

39. (Withdrawn -- currently amended) The method of claim 12 or 37 wherein said mutation is a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons 857, 1041, 1044, [[and]] 1049, and 1114 of the VEGFR-3 encoding sequence set forth in SEQ ID NO: 1.

40. (Currently amended) The method of claim 12 or 37 wherein said mutation is a missense mutation in a VEGFR-3 allele at a position corresponding to codon 1114 of the VEGFR-3-encoding sequence set forth in SEQ ID NO: 1.

41. (Currently amended) The method of claim 12 or 37, wherein the wildtype VEGFR-3 allele comprises the VEGFR-3 coding sequence set forth in SEQ ID NO: 1.

42. (Previously presented) The method of claim 12, wherein said administering of said therapeutically effective amount of said growth factor product induces VEGF-3 signaling in the lymphatic endothelia of the patient.

43. (Previously presented) The method of claim 37, wherein said administering of said therapeutically effective amount of said growth factor product induces VEGFR-3 signaling in the lymphatic endothelia of the patient.

44. (Currently amended) The method of claim 12 or 37, wherein said administering of said therapeutically effective amount of said growth factor product reduces edema in a limb of said patient.

45. (Currently amended) The method of claim 12 or 37, wherein said administering of said therapeutically effective amount of said growth factor product reduces accumulation of lymph fluids in said patient.

46. (Canceled)

47. (Currently amended) The method of claim 12 or 37, wherein said ~~growth factor product is~~ VEGF-C gene therapy product comprises a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising a nucleotide sequence that encodes a polypeptide comprising SEQ ID NO: 4;

(b) a polynucleotide comprising a nucleotide sequence that encodes a polypeptide that comprises a continuous portion of SEQ ID NO: 4 sufficient to permit the encoded polypeptide to bind wildtype humanVEGFR-3 and stimulate VEGFR-3 phosphorylation in cells that express wildtype human VEGFR-3;

(c) a polynucleotide comprising a nucleotide sequence that encodes an analog of the polypeptide encoded by (a) or (b), wherein the analog has up to 25 amino acids added, deleted, or substituted with another amino acid, compared to the amino acid sequence encoded by (a) or (b), and wherein the analog retains the ability to bind and stimulate phosphorylation of wildtype human VEGFR-3.

48. (Currently amended) The method of claim 12 or 37 [[47]], wherein said VEGF-C gene therapy product comprises a polynucleotide that comprises a nucleotide sequence that will hybridize to a nucleic acid that is complementary to SEQ ID NO: 3 under the following exemplary stringent hybridization conditions:

hybridization at hybridization at 42° C in 50% formamide, 5x SSC, 20 mM $Na{\cdot}PO_4$, pH 6.8; and

washing in 1x SSC at 55°C for 30 minutes;

wherein the nucleotide sequence encodes a polypeptide that binds VEGFR-3 and ~~is a mutant VEGF-C that~~ stimulates phosphorylation of wildtype human VEGFR-3.

49. (Currently amended) The method of claim 47 [[48]], wherein said ~~mutant~~ VEGF-C gene therapy product comprises a polynucleotide that comprises a nucleotide sequence that encodes [[is]] a VEGF-CΔC_{156} polypeptide.

50. (Currently amended) The method of claim 47, wherein said VEGF-C gene therapy product is administered via intravenous injection.

51. (Currently amended) The method of claim 47, wherein said VEGF-C gene therapy product is administered via intramuscular injection.

52. (New) The method of claim 39, wherein said mutation is a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons 857, 1041, 1044, and 1049 of the VEGFR-3 encoding sequence set forth in SEQ ID NO: 1.

53. (New) The method of claim 12 or 37, wherein said VEGF-C gene therapy product comprises a polynucleotide that comprises a nucleotide sequence that encodes a polypeptide that comprises at least amino acids 131-211 of SEQ ID NO: 4 and that binds wildtype human VEGFR-3 and stimulates VEGFR-3 phosphorylation in cells that express wildtype human VEGFR-3.

54. (New) The method of claim 12 or 37, wherein said VEGF-C gene therapy product comprises a a polynucleotide that comprises a nucleotide sequence that encodes a polypeptide that comprises at least amino acids 113-211 of SEQ ID NO: 4 and that binds wildtype human VEGFR-3 and stimulates VEGFR-3 phosphorylation in cells that express wildtype human VEGFR-3.

55. (New) The method of claim 12 or 37, wherein said VEGF-C gene therapy product comprises a a polynucleotide that comprises a nucleotide sequence that encodes a continuous portion of SEQ ID NO: 4 that has, as its amino terminus, an amino acid selected from the group consisting of positions 30-131 of SEQ ID NO: 4, and as its carboxyl terminus, an amino acid selected from the group consisting of positions 211-419 of SEQ ID NO: 4, wherein the polypeptide binds wildtype human VEGFR-3 and stimulates VEGFR-3 phosphorylation in cells that express wildtype human VEGFR-3.

56. (New) The method of claim 47, wherein the VEGF-C gene therapy product further comprises a nucleotide sequence that encodes a secretory signal peptide fused in-frame with the sequence that encodes the polypeptide.

57. (New) The method of claim 47, wherein the VEGF-Cgene therapy product further comprises at least one sequence selected from the group consisting of a promoter, an enhancer, and a polyadenylation signal sequence.

58. (New) The method of claim 47, wherein said VEGF-C gene therapy product comprises vector that comprises the polynucleotide.

59. (New) The method of claim 58, wherein said vector comprises a replication-deficient retroviral vector.

60. (New) The method of claim 58, wherein said vector comprises a vector selected from the group consisting of lentivirus vectors, adeno-associated viral vectors, and adenoviral vectors.

61. (New) The method of claim 47, wherein the administering step comprises administering a composition that comprises the VEGF-C gene therapy product and a pharmaceutically acceptable carrier.